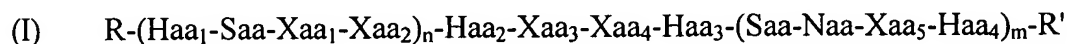


IN THE CLAIMS:

Please amend claims set forth below.

1. (Currently Amended) A conformationally constrained compound or a pharmaceutically acceptable salt or prodrug thereof, the compound comprising an amino acid sequence (I):



[SEQ ID NO: 1-3]

wherein Haa₁, Haa₂, Haa₃ and Haa₄ are each independently an amino acid residue with a hydrophobic side chain or when n and m are both 1, one of Haa₁, Haa₂ and Haa₄ is optionally Xaa₁;

each Saa is an amino acid residue with a small side chain;

Naa is an amino acid residue with a negatively charged side chain;

Xaa₁, Xaa₂, Xaa₃, Xaa₄ and Xaa₅ are each independently an amino acid residue, Zaa₁ or Zaa₂;

R is H, an N-terminal capping group or an oligopeptide optionally capped by an N-terminal capping group;

R' is H, a C-terminal capping group or an oligopeptide optionally capped by a C-terminal capping group; and

m and n are 0 or 1, provided that at least one of m and n is 1;

wherein a conformational constraint is provided by a linker (L) which tethers two amino acid residues, Zaa₁ and Zaa₂, in the sequence.

2. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 1 wherein all of Haa₁, Haa₂, Haa₃ and Haa₄ are amino acid residues with a hydrophobic side chain.

3. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 1 wherein Haa₁, Haa₂, Haa₃ and Haa₄ are independently selected from L-phenylalanine, L-isoleucine, L-leucine, L-valine, L-methionine and L-tyrosine.

4. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 1 wherein Haa₂ is L-leucine.
5. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 1 wherein each Saa is independently selected from glycine, L-alanine, L-serine, L-cysteine and aminoisobutyric acid.
6. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 1 wherein Naa is an L-aspartic acid or an L-glutamic acid residue.
7. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 1 wherein R is an N-terminal capping group or an oligopeptide having 1 to 10 amino acid residues selected from Xaa₁, optionally capped with an N-terminal capping group.
8. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 7 wherein R is an N-terminal capping group selected from acyl and N-succinate.
9. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 1 wherein R' is a C-terminal capping group or an oligopeptide having 1 to 10 amino acid residues selected from Xaa₁, optionally capped with a C-terminal capping group.
10. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 9, wherein the C-terminal capping group is NH₂.
11. (Original) A conformationally constrained compound or pharmaceutically acceptable salt

or prodrug thereof according to claim 1, wherein Xaa₁, Xaa₂, Xaa₃, Xaa₄ and Xaa₅ are independently selected from L-alanine, L-arginine, L-asparagine, L-aspartic acid, L-cysteine, L-glutamine, L-glutamic acid, L-glycine, L-histidine, L-isoleucine, L-leucine, L-lysine, L-methionine, L-phenylalanine, L-proline, L-serine, L-threonine, L-tryptophan, L-tyrosine and L-valine.

12. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 1 wherein the linker (L) tethers two non-adjacent amino acids in an i(i+7) relationship where the first end of the linker is attached to a first amino acid residue (Zaa₁) at a first position and the other end of the linker is attached to a second amino acid residue (Zaa₂) which is positioned 7 amino acids after Zaa₁.

13. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 1 wherein L is 4 to 8 atoms in length.

14. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 12 wherein Zaa₁ is located before Haa₁ at the N-terminal of the sequence and Zaa₂ is located between Haa₂ and Haa₃.

15. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 12 wherein Zaa₁ is located between Haa₁ and Haa₂ and Zaa₂ is located between Haa₃ and Haa₄.

16. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 12 wherein Zaa₁ is located between Haa₂ and Haa₃ and Zaa₂ is located after Haa₄ at the C-terminal end of the amino acid sequence.

17. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 1 wherein Zaa₁ and Zaa₂ are independently selected from L-aspartic acid, L-glutamic acid, L-lysine, L-ornithine, D-aspartic acid, D-glutamic acid, D-

lysine, D-ornithine, L- β -homoaspartic acid, L- β -homoglutamic acid, L- β -homolysine, L- α -methylasspartic acid, L- α -methylglutamic acid, L- α -methyllysine, L- α -methylornithine, D- α -methylasspartic acid, D- α -methylglutamic acid, D- α -methyllysine and L- α -methylornithine.

18. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 17 wherein Zaa₁ and Zaa₂ are independently selected from L-aspartic acid, L-glutamic acid, L-lysine and L-ornithine.

19. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 18 wherein Zaa₁ and Zaa₂ are independently selected from L-aspartic acid and L-glutamic acid.

20. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 1 wherein Zaa₁ and Zaa₂ have side chains containing a carboxylic acid and the linker is selected from the group consisting of -NH(CH₂)₄NH-, -NH(CH₂)₅NH-, -NH(CH₂)₆NH-, -NH(CH₂)₇NH-, -NH(CH₂)₂O(CH₂)₂NH-, -NH(CH₂)₂N⁺H₂(CH₂)₂NH-, -NH(CH₂)₂S(CH₂)₂NH-, -NHCH₂C(=O)NH(CH₂)₂NH-, -NH(CH₂)₂NHC(=O)CH₂NH-, -NH(CH₂)₂SS(CH₂)₂NH-, -NH(CH₂)₂O(CH₂)₃NH-, -NH(CH₂)₂N⁺H₂(CH₂)₃NH-, -NH(CH₂)₂S(CH₂)₃NH-, -NH(CH₂)₂C(=O)NH(CH₂)₂NH-, -NH(CH₂)₂NHC(=O)(CH₂)₂NH-, -NHCH₂C(=O)NH(CH₂)₃NH-, -NH(CH₂)₃NHC(=O)CH₂NH-, -NHCH₂C(=O)NH(CH₂)₄NH-, -NH(CH₂)₄NHC(=O)CH₂NH-, -NH(CH₂)₂C(=O)NH(CH₂)₃NH-, -NH(CH₂)₃NHC(=O)(CH₂)₂NH-, -NH(CH₂)₃C(=O)NH(CH₂)₂NH- and -NH(CH₂)₂NHC(=O)(CH₂)₃NH-.

21. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 20 wherein the linker is selected from the group consisting of -NH(CH₂)₅NH-, -NH(CH₂)₆NH-, -NH(CH₂)₇NH-, -NHCH₂C(=O)NH(CH₂)₂NH-, -NH(CH₂)₂NHC(=O)CH₂NH-, -NH(CH₂)₂O(CH₂)₃NH- and -NH(CH₂)₂C(=O)NH(CH₂)₂NH-.

22. (Original) A conformationally constrained compound or pharmaceutically acceptable salt

or prodrug thereof according to claim 20 wherein the linker is selected from the group consisting of $-\text{NH}(\text{CH}_2)_5\text{NH}-$ and $-\text{NHCH}_2\text{C}(=\text{O})\text{NH}(\text{CH}_2)_2\text{NH}-$.

23. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 1 wherein Zaa₁ and Zaa₂ have side chains containing an amino group and the linker is selected from the group consisting of $-\text{C}(=\text{O})(\text{CH}_2)_4\text{C}(=\text{O})-$, $-\text{C}(=\text{O})(\text{CH}_2)_5\text{C}(=\text{O})-$, $-\text{C}(=\text{O})(\text{CH}_2)_6\text{C}(=\text{O})-$, $-\text{C}(=\text{O})(\text{CH}_2)_7\text{C}(=\text{O})-$, $-\text{C}(=\text{O})(\text{CH}_2)_2\text{O}(\text{CH}_2)_2\text{C}(=\text{O})-$, $-\text{C}(=\text{O})(\text{CH}_2)\text{N}^+\text{H}_2(\text{CH}_2)_2\text{C}(=\text{O})-$, $-\text{C}(=\text{O})(\text{CH}_2)\text{S}(\text{CH}_2)_2\text{C}(=\text{O})-$, $-\text{C}(=\text{O})\text{CH}_2\text{C}(=\text{O})\text{NH}(\text{CH}_2)_2\text{C}(=\text{O})-$, $-\text{C}(=\text{O})(\text{CH}_2)_2\text{NHC}(=\text{O})\text{CH}_2\text{C}(=\text{O})-$, $-\text{C}(=\text{O})(\text{CH}_2)_2\text{SS}(\text{CH}_2)_2\text{C}(=\text{O})-$, $-\text{C}(=\text{O})(\text{CH}_2)_2\text{O}(\text{CH}_2)_3\text{C}(=\text{O})-$, $-\text{C}(=\text{O})(\text{CH}_2)_2\text{N}^+\text{H}_2(\text{CH}_2)_3\text{C}(=\text{O})-$, $-\text{C}(=\text{O})(\text{CH}_2)_2\text{S}(\text{CH}_2)_3\text{C}(=\text{O})-$, $-\text{C}(=\text{O})(\text{CH}_2)_2\text{C}(=\text{O})\text{NH}(\text{CH}_2)_2\text{C}(=\text{O})-$, $-\text{C}(=\text{O})(\text{CH}_2)_2\text{NHC}(=\text{O})(\text{CH}_2)_2\text{C}(=\text{O})-$, $-\text{C}(=\text{O})\text{CH}_2\text{C}(=\text{O})\text{NH}(\text{CH}_2)_3\text{C}(=\text{O})-$, $-\text{C}(=\text{O})(\text{CH}_2)_3\text{NHC}(=\text{O})\text{CH}_2\text{C}(=\text{O})-$, $-\text{C}(=\text{O})\text{CH}_2\text{C}(=\text{O})\text{NH}(\text{CH}_2)_4\text{C}(=\text{O})-$, $-\text{C}(=\text{O})(\text{CH}_2)_4\text{NHC}(=\text{O})\text{CH}_2\text{C}(=\text{O})-$, $-\text{C}(=\text{O})(\text{CH}_2)_2\text{C}(=\text{O})\text{NH}(\text{CH}_2)_3\text{C}(=\text{O})-$, $-\text{C}(=\text{O})(\text{CH}_2)_3\text{NHC}(=\text{O})(\text{CH}_2)_2\text{C}(=\text{O})-$, $-\text{C}(=\text{O})(\text{CH}_2)_3\text{C}(=\text{O})\text{NH}(\text{CH}_2)_2\text{C}(=\text{O})-$ and $-\text{C}(=\text{O})(\text{CH}_2)_2\text{NHC}(=\text{O})(\text{CH}_2)_3\text{C}(=\text{O})-$.

24. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 23 wherein the linker is selected from the group consisting of $-\text{C}(=\text{O})(\text{CH}_2)_5\text{C}(=\text{O})-$, $-\text{C}(=\text{O})(\text{CH}_2)_6\text{C}(=\text{O})-$, $-\text{C}(=\text{O})(\text{CH}_2)_7\text{C}(=\text{O})-$, $-\text{C}(=\text{O})\text{CH}_2\text{C}(=\text{O})\text{NH}(\text{CH}_2)_2\text{C}(=\text{O})-$, $-\text{C}(=\text{O})(\text{CH}_2)_2\text{NHC}(=\text{O})\text{CH}_2\text{C}(=\text{O})-$, $-\text{C}(=\text{O})(\text{CH}_2)_2\text{O}(\text{CH}_2)_3\text{C}(=\text{O})-$ and $-\text{C}(=\text{O})(\text{CH}_2)_2\text{C}(=\text{O})\text{NH}(\text{CH}_2)_2\text{C}(=\text{O})-$.

25. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 23 wherein the linker is selected from the group consisting of $-\text{C}(=\text{O})(\text{CH}_2)_5\text{C}(=\text{O})-$ and $-\text{C}(=\text{O})\text{CH}_2\text{C}(=\text{O})\text{NH}(\text{CH}_2)_2\text{C}(=\text{O})-$.

26. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 1 wherein Zaa₁ has a side chain containing an amino group and Zaa₂ has a side chain containing a carboxylic acid and the linker is selected

-C(=O)(CH₂)₄NH-, -C(=O)(CH₂)₅NH-, -C(=O)(CH₂)₆NH-, -C(=O)(CH₂)₇NH-,
-C(=O)(CH₂)₂O(CH₂)₂NH-, -C(=O)(CH₂)N⁺H₂(CH₂)₂NH-, -C(=O)(CH₂)S(CH₂)₂NH-,
-C(=O)CH₂C(=O)NH(CH₂)₂NH-, -C(=O)(CH₂)₂NHC(=O)CH₂NH-, -C(=O)(CH₂)₂SS(CH₂)₂-
NH-, -C(=O)(CH₂)₂O(CH₂)₃NH-, -C(=O)(CH₂)₂N⁺H₂(CH₂)₃NH-, -C(=O)(CH₂)₂S(CH₂)₃NH-,
-C(=O)(CH₂)₂C(=O)NH(CH₂)₂NH-, -C(=O)(CH₂)₂NHC(=O)(CH₂)₂NH-,
-C(=O)CH₂C(=O)NH(CH₂)₃NH-, -C(=O)(CH₂)₃NHC(=O)CH₂NH-,
-C(=O)CH₂C(=O)NH(CH₂)₄NH-, -C(=O)(CH₂)₄NHC(=O)CH₂NH-,
-C(=O)(CH₂)₂C(=O)NH(CH₂)₃NH-, -C(=O)(CH₂)₃NHC(=O)(CH₂)₂NH-,
-C(=O)(CH₂)₃C(=O)NH(CH₂)₂NH- and -C(=O)(CH₂)₂NHC(=O)(CH₂)₃NH-.

27. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 26 wherein the linker is selected from the group consisting of -C(=O)(CH₂)₅NH-, -C(=O)(CH₂)₆NH-, -C(=O)(CH₂)₇NH-, -C(=O)CH₂C(=O)NH(CH₂)₂NH-, -C(=O)(CH₂)₂NHC(=O)CH₂NH-, -C(=O)(CH₂)₂O(CH₂)₃NH- and -C(=O)(CH₂)₂C(=O)NH(CH₂)₂NH-.

28. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 26 wherein the linker is selected from the group consisting of -C(=O)(CH₂)₅NH- and -C(=O)CH₂C(=O)NH(CH₂)₂NH-.

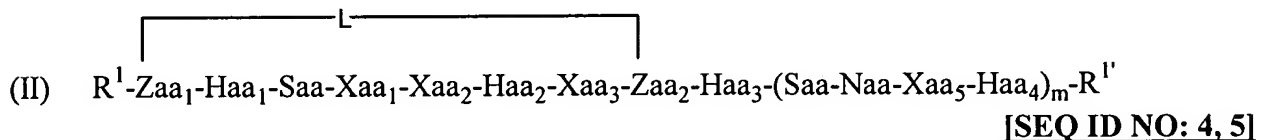
29. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 1 wherein Zaa₁ has a side chain containing a carboxylic acid and Zaa₂ has a side chain containing an amino group and the linker is selected from the group consisting of -NH(CH₂)₄C(=O)-, -NH(CH₂)₅C(=O)-, -NH(CH₂)₆C(=O)-, -NH(CH₂)₇C(=O)-, -NH(CH₂)₂O(CH₂)₂C(=O)-, -NH(CH₂)N⁺H₂(CH₂)₂C(=O)-, -NH(CH₂)S(CH₂)₂C(=O)-, -NHCH₂C(=O)NH(CH₂)₂C(=O)-, -NH(CH₂)₂NHC(=O)CH₂C(=O)-, -NH(CH₂)₂SS(CH₂)₂C(=O)-, -NH(CH₂)₂O(CH₂)₃C(=O)-, -NH(CH₂)₂N⁺H₂(CH₂)₃C(=O)-, -NH(CH₂)₂S(CH₂)₃C(=O)-, -NH(CH₂)₂C(=O)NH(CH₂)₂C(=O)-, -NH(CH₂)₂NHC(=O)(CH₂)₂C(=O)-, -NHCH₂C(=O)NH(CH₂)₃C(=O)-, -NH(CH₂)₃NHC(=O)CH₂C(=O)-, -NHCH₂C(=O)NH(CH₂)₄C(=O)-,

-NH(CH₂)₄NHC(=O)CH₂C(=O)-, -NH(CH₂)₂C(=O)NH(CH₂)₃C(=O)-,
-NH(CH₂)₃NHC(=O)(CH₂)₂C(=O)-, -NH(CH₂)₃C(=O)NH(CH₂)₂C(=O)-.

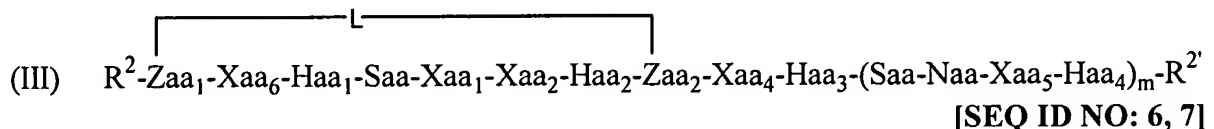
30. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 29 wherein the linker is selected from the group consisting of -NH(CH₂)₅C(=O)-, -NH(CH₂)₆C(=O)-, -NH(CH₂)₇C(=O)-, -NHCH₂C(=O)NH(CH₂)₂C(=O)-, -NH(CH₂)₂NHC(=O)CH₂C(=O)-, -NH(CH₂)₂O(CH₂)₃C(=O)- and -NH(CH₂)₂C(=O)NH(CH₂)₂C(=O)-.

31. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 29 wherein the linker is selected from the group consisting of -NH(CH₂)₅C(=O)- and -NHCH₂C(=O)NH(CH₂)₂C(=O)-.

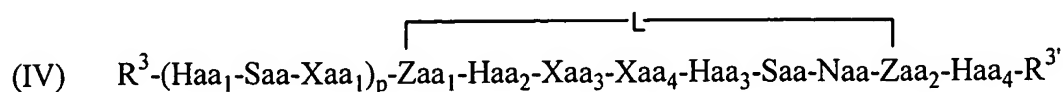
32. (Currently Amended) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 1, of any one of formulae (II) to (VI):



wherein Haa₁, Haa₂, Haa₃, Haa₄, Xaa₁, Xaa₂, Xaa₃, Xaa₅, Saa, Naa and L are as defined above for formula (I), m is 0 or 1, R¹ and R^{1'} are as defined above for R and R' in formula (I), Zaa₁-L-Zaa₂ represents two amino acid residues with their side chains bridged by a linker L;

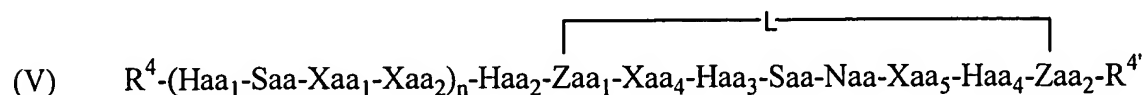


wherein Haa₁, Haa₂, Haa₃, Haa₄, Xaa₁, Xaa₂, Xaa₄, Xaa₅, Saa, Naa and L are as defined above for formula (I), Xaa₆ is an amino acid residue as defined for Xaa₁ above; m is 0 or 1, R² and R^{2'} are as defined above for R and R' in formula (I), Zaa₁-L-Zaa₂ represents two amino acid residues with their side chains bridged by a linker L;



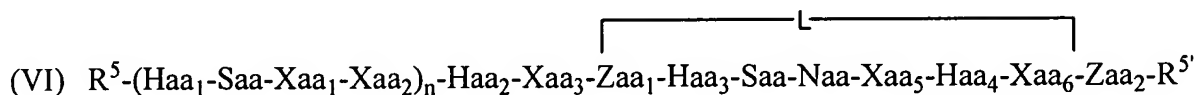
[SEQ ID NO: 8, 9]

wherein Haa₁, Haa₂, Haa₃, Haa₄, Xaa₁, Xaa₃, Xaa₄, Saa, Naa and L are as defined above for formula (I), p is 0 or 1, R³ and R^{3'} are as defined above for R and R' in formula (I), Zaa₁-L-Zaa₂ represents two amino acid residues with their side chains bridged by a linker L;



[SEQ ID NO: 10, 11]

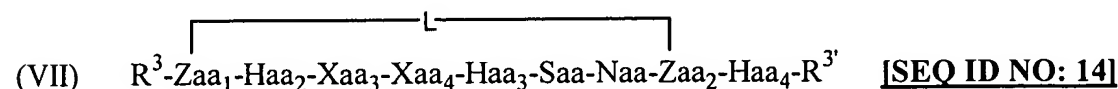
wherein Haa₁, Haa₂, Haa₃, Haa₄, Xaa₁, Xaa₂, Xaa₄, Xaa₅, Saa, Naa and L are as defined above in formula (I), n is 0 or 1, R⁴ and R^{4'} are as defined above for R and R' in formula (I), Zaa₁-L-Zaa₂ represents two amino acid residues with their side chains bridged by a linker L; and



[SEQ ID NO: 12, 13]

wherein Haa₁, Haa₂, Haa₃, Haa₄, Xaa₁, Xaa₂, Xaa₃, Xaa₅, Saa, Naa and L are as defined above for formula (I), Xaa₆ is an amino acid residue as defined for Xaa₁ above; n is 0 or 1, R⁵ and R^{5'} are as defined above for R and R' in formula (I), Zaa₁-L-Zaa₂ represents two amino acid residues with their side chains bridged by a linker L; or a pharmaceutically acceptable salt or prodrug thereof.

33. (Currently Amended) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 32 having structural formula (VII):

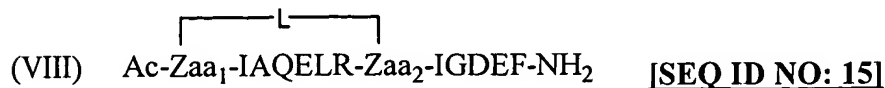


[SEQ ID NO: 14]

wherein Zaa₁, Haa₂, Xaa₃, Xaa₄, Haa₃, Saa, Naa, Zaa₂, Haa₄, R³, R^{3'} and L are defined above in formula (IV).

34. (Currently Amended) A conformationally constrained compound or pharmaceutically

acceptable salt or prodrug thereof according to claim 1 having structural formula (VIII):



where Zaa₁ and Zaa₂ are selected from L-aspartic acid, L-glutamic acid; and

L is selected from -NH(CH₂)₄NH-, -NH(CH₂)₅NH-, -NH(CH₂)₆NH-, -NH(CH₂)₇NH-,
-NH(CH₂)₂O(CH₂)₂NH-, -NH(CH₂)N⁺H₂(CH₂)₂NH-, -NH(CH₂)S(CH₂)₂NH-,
-NHCH₂C(=O)NH(CH₂)₂NH-, -NH(CH₂)₂NHC(=O)CH₂NH-, -NH(CH₂)₂SS(CH₂)₂NH-,
-NH(CH₂)₂O(CH₂)₃NH-, -NH(CH₂)₂N⁺H₂(CH₂)₃NH-, -NH(CH₂)₂S(CH₂)₃NH-,
-NH(CH₂)₂C(=O)NH(CH₂)₂NH- and -NH(CH₂)₂NHC(=O)(CH₂)₂NH-; or

where Zaa₁ and Zaa₂ are selected from L-lysine and ornithine; and

L is selected from -C(=O)(CH₂)₄C(=O)-, -C(=O)(CH₂)₅C(=O)-, -C(=O)(CH₂)₆C(=O)-,
-C(=O)(CH₂)₇C(=O)-, -C(=O)(CH₂)₂O(CH₂)₂C(=O)-, -C(=O)(CH₂)N⁺H₂(CH₂)₂C(=O)-,
-C(=O)(CH₂)S(CH₂)₂C(=O)-, -C(=O)CH₂C(=O)NH(CH₂)₂C(=O)-,
-C(=O)(CH₂)₂NHC(=O)CH₂C(=O)-, -C(=O)(CH₂)₂SS(CH₂)₂C(=O)-,
-C(=O)(CH₂)₂O(CH₂)₃C(=O)-, -C(=O)(CH₂)₂N⁺H₂(CH₂)₃C(=O)-, -C(=O)(CH₂)₂S(CH₂)₃C(=O)-,
-C(=O)(CH₂)₂C(=O)NH(CH₂)₂C(=O)- and -C(=O)(CH₂)₂NHC(=O)(CH₂)₂C(=O)-; or

where Zaa₁ is selected from L-aspartic acid, L-glutamic acid and Zaa₂ is selected from L-lysine and ornithine; and

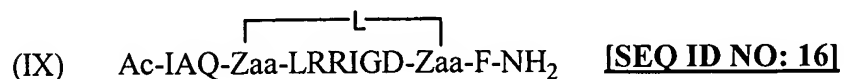
L is selected from -NH(CH₂)₄C(=O)-, -NH(CH₂)₅C(=O)-, -NH(CH₂)₆C(=O)-, -NH(CH₂)₇C(=O)-,
-NH(CH₂)₂O(CH₂)₂C(=O)-, -NH(CH₂)N⁺H₂(CH₂)₂C(=O)-, -NH(CH₂)S(CH₂)₂C(=O)-,
-NHCH₂C(=O)NH(CH₂)₂C(=O)-, -NH(CH₂)₂NHC(=O)CH₂C(=O)-, -NH(CH₂)₂SS(CH₂)₂C(=O)-,
-NH(CH₂)₂O(CH₂)₃C(=O)-, -NH(CH₂)₂N⁺H₂(CH₂)₃C(=O)-, -NH(CH₂)₂S(CH₂)₃C(=O)-,
-NH(CH₂)₂C(=O)NH(CH₂)₂C(=O)- and -NH(CH₂)₂NHC(=O)(CH₂)₂C(=O)-; or

where Zaa₁ is selected from L-lysine and ornithine and Zaa₂ is selected from L-aspartic acid, L-glutamic acid; and

L is selected from -C(=O)(CH₂)₄NH-, -C(=O)(CH₂)₅NH-, -C(=O)(CH₂)₆NH-, -C(=O)(CH₂)₇NH-,
-C(=O)(CH₂)₂O(CH₂)₂NH-, -C(=O)(CH₂)N⁺H₂(CH₂)₂NH-, -C(=O)(CH₂)S(CH₂)₂NH-,
-C(=O)CH₂C(=O)NH(CH₂)₂NH-, -C(=O)(CH₂)₂NHC(=O)CH₂NH-, -C(=O)(CH₂)₂SS(CH₂)₂NH-,
-C(=O)(CH₂)₂O(CH₂)₃NH-, -C(=O)(CH₂)₂N⁺H₂(CH₂)₃NH-, -C(=O)(CH₂)₂S(CH₂)₃NH-,

$-C(=O)(CH_2)_2C(=O)NH(CH_2)_2NH-$ and $-C(=O)(CH_2)_2NHC(=O)(CH_2)_2NH-$.

35. (Currently Amended) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 1 having structural formula (IX):



where Zaa₁ and Zaa₂ are selected from L-aspartic acid, L-glutamic acid; and

L is selected from $-NH(CH_2)_4NH-$, $-NH(CH_2)_5NH-$, $-NH(CH_2)_6NH-$, $-NH(CH_2)_7NH-$, $-NH(CH_2)_2O(CH_2)_2NH-$, $-NH(CH_2)N^+H_2(CH_2)_2NH-$, $-NH(CH_2)S(CH_2)_2NH-$, $-NHCH_2C(=O)NH(CH_2)_2NH-$, $-NH(CH_2)_2NHC(=O)CH_2NH-$, $-NH(CH_2)_2SS(CH_2)_2NH-$, $-NH(CH_2)_2O(CH_2)_3NH-$, $-NH(CH_2)_2N^+H_2(CH_2)_3NH-$, $-NH(CH_2)_2S(CH_2)_3NH-$, $-NH(CH_2)_2C(=O)NH(CH_2)_2NH-$, $-NH(CH_2)_2NHC(=O)(CH_2)_2NH-$, $-NHCH_2C(=O)NH(CH_2)_3NH-$, $-NH(CH_2)_3NHC(=O)CH_2NH-$, $-NHCH_2C(=O)NH(CH_2)_4NH-$, $-NH(CH_2)_4NHC(=O)CH_2NH-$, $-NH(CH_2)_2C(=O)NH(CH_2)_3NH-$, $-NH(CH_2)_3NHC(=O)(CH_2)_2NH-$, $-NH(CH_2)_3C(=O)NH(CH_2)_2NH-$ and $-NH(CH_2)_2NHC(=O)(CH_2)_3NH-$; or

where Zaa₁ and Zaa₂ are selected from L-lysine and ornithine; and

L is selected from $-C(=O)(CH_2)_4C(=O)-$, $-C(=O)(CH_2)_5C(=O)-$, $-C(=O)(CH_2)_6C(=O)-$, $-C(=O)(CH_2)_7C(=O)-$, $-C(=O)(CH_2)_2O(CH_2)_2C(=O)-$, $-C(=O)(CH_2)N^+H_2(CH_2)_2C(=O)-$, $-C(=O)(CH_2)S(CH_2)_2C(=O)-$, $-C(=O)CH_2C(=O)NH(CH_2)_2C(=O)-$, $-C(=O)(CH_2)_2NHC(=O)CH_2C(=O)-$, $-C(=O)(CH_2)_2SS(CH_2)_2C(=O)-$, $-C(=O)(CH_2)_2O(CH_2)_3C(=O)-$, $-C(=O)(CH_2)_2N^+H_2(CH_2)_3C(=O)-$, $-C(=O)(CH_2)_2S(CH_2)_3C(=O)-$, $-C(=O)(CH_2)_2C(=O)NH(CH_2)_2C(=O)-$, $-C(=O)(CH_2)_2NHC(=O)(CH_2)_2C(=O)-$, $-C(=O)CH_2C(=O)NH(CH_2)_3C(=O)-$, $-C(=O)(CH_2)_3NHC(=O)CH_2C(=O)-$, $-C(=O)CH_2C(=O)NH(CH_2)_4C(=O)-$, $-C(=O)(CH_2)_4NHC(=O)CH_2C(=O)-$, $-C(=O)(CH_2)_2C(=O)NH(CH_2)_3C(=O)-$, $-C(=O)(CH_2)_3NHC(=O)(CH_2)_2C(=O)-$, $-C(=O)(CH_2)_3C(=O)NH(CH_2)_2C(=O)-$ and $-C(=O)(CH_2)_2NHC(=O)(CH_2)_3C(=O)-$; or

where Zaa₁ is selected from L-aspartic acid, L-glutamic acid and Zaa₂ is selected from L-lysine and ornithine; and

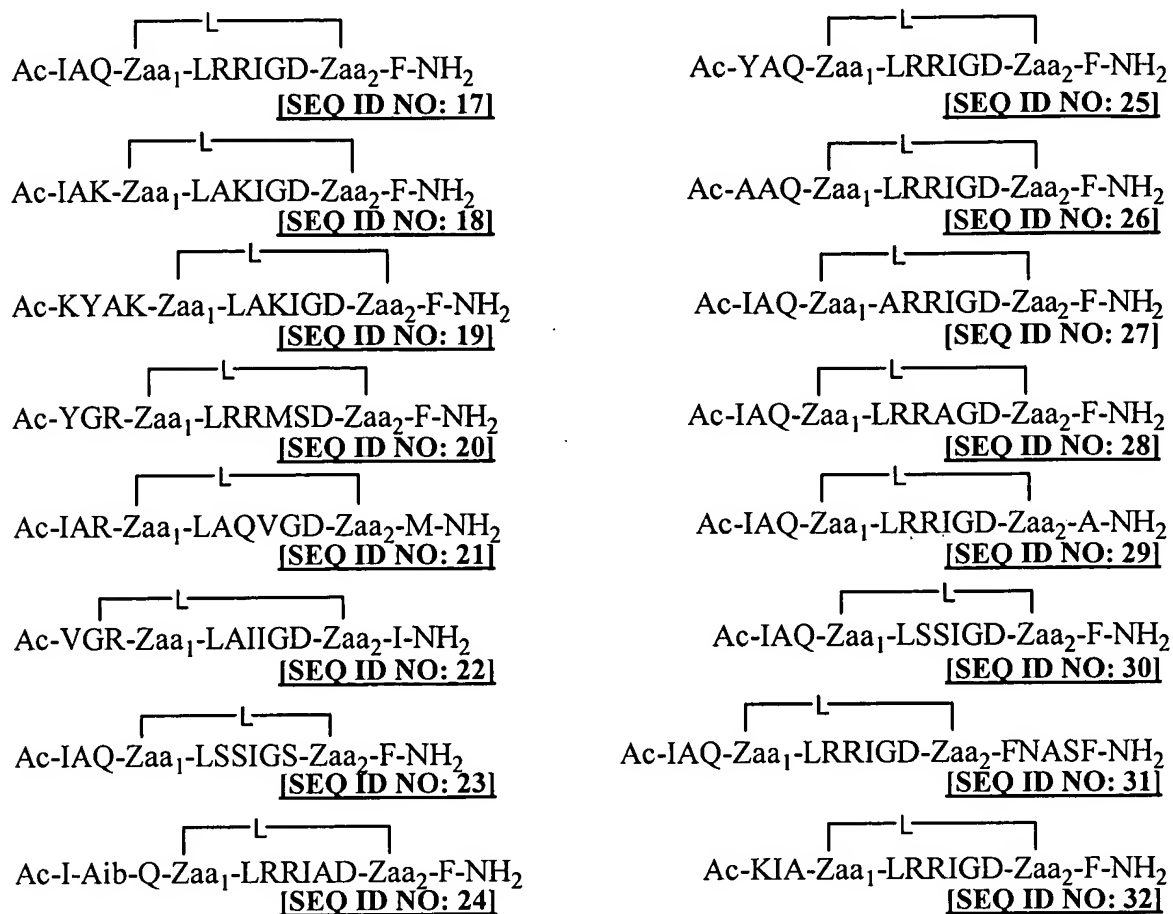
L is selected from $-NH(CH_2)_4C(=O)-$, $-NH(CH_2)_5C(=O)-$, $-NH(CH_2)_6C(=O)-$, $-NH(CH_2)_7C(=O)-$

, -NH(CH₂)₂O(CH₂)₂C(=O)-, -NH(CH₂)N⁺H₂(CH₂)₂C(=O)-, -NH(CH₂)S(CH₂)₂C(=O)-,
-NHCH₂C(=O)NH(CH₂)₂C(=O)-, -NH(CH₂)₂NHC(=O)CH₂C(=O)-, -NH(CH₂)₂SS(CH₂)₂C(=O)-,
-NH(CH₂)₂O(CH₂)₃C(=O)-, -NH(CH₂)₂N⁺H₂(CH₂)₃C(=O)-, -NH(CH₂)₂S(CH₂)₃C(=O)-,
-NH(CH₂)₂C(=O)NH(CH₂)₂C(=O)-, -NH(CH₂)₂NHC(=O)(CH₂)₂C(=O)-
-NHCH₂C(=O)NH(CH₂)₃C(=O)-, -NH(CH₂)₃NHC(=O)CH₂C(=O)-,
-NHCH₂C(=O)NH(CH₂)₄C(=O)-, -NH(CH₂)₄NHC(=O)CH₂C(=O)-,
-NH(CH₂)₂C(=O)NH(CH₂)₃C(=O)-, -NH(CH₂)₃NHC(=O)(CH₂)₂C(=O)-,
-NH(CH₂)₃C(=O)NH(CH₂)₂C(=O)- and -NH(CH₂)₂NHC(=O)(CH₂)₃C(=O)-; or

where Zaa₁ is selected from L-lysine and ornithine and Zaa₂ is selected from L-aspartic acid, L-glutamic acid; and

L is selected from -C(=O)(CH₂)₄NH-, -C(=O)(CH₂)₅NH-, -C(=O)(CH₂)₆NH-, -C(=O)(CH₂)₇NH-,
-C(=O)(CH₂)₂O(CH₂)₂NH-, -C(=O)(CH₂)N⁺H₂(CH₂)₂NH-, -C(=O)(CH₂)S(CH₂)₂NH-,
-C(=O)CH₂C(=O)NH(CH₂)₂NH-, -C(=O)(CH₂)₂NHC(=O)CH₂NH-, -C(=O)(CH₂)₂SS(CH₂)₂NH-,
-C(=O)(CH₂)₂O(CH₂)₃NH-, -C(=O)(CH₂)₂N⁺H₂(CH₂)₃NH-, -C(=O)(CH₂)₂S(CH₂)₃NH-,
-C(=O)(CH₂)₂C(=O)NH(CH₂)₂NH-, -C(=O)(CH₂)₂NHC(=O)(CH₂)₂NH-,
-C(=O)CH₂C(=O)NH(CH₂)₃NH-, -C(=O)(CH₂)₃NHC(=O)CH₂NH-,
-C(=O)CH₂C(=O)NH(CH₂)₄NH-, -C(=O)(CH₂)₄NHC(=O)CH₂NH-,
-C(=O)(CH₂)₂C(=O)NH(CH₂)₃NH-, -C(=O)(CH₂)₃NHC(=O)(CH₂)₂NH-,
-C(=O)(CH₂)₃C(=O)NH(CH₂)₂NH- and -C(=O)(CH₂)₂NHC(=O)(CH₂)₃NH-.

36. (Currently Amended) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 1 selected from the group consisting of:

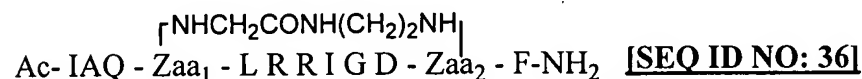
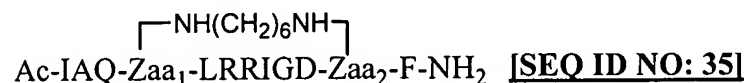
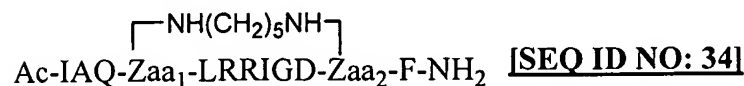


wherein Zaa₁ and Zaa₂ are as defined in claim 17 and L is a linker which tethers Zaa₁ and Zaa₂.

37. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 36 wherein Zaa₁ and Zaa₂ are independently selected from L-aspartic acid and L-glutamic acid and L is selected from the group consisting of -NH(CH₂)₅NH-, -NH(CH₂)₆NH-, -NH(CH₂)₇NH-, -NHCH₂(=O)NH(CH₂)₂NH-, -NH(CH₂)₂NHC(=O)CH₂NH-, -NH(CH₂)₂O(CH₂)₃NH- and -NH(CH₂)₂C(=O)NH(CH₂)₂NH-.

38. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 37 wherein L is selected from the group consisting of -NH(CH₂)₅NH- and -NHCH₂C(=O)NH(CH₂)₂NH-.

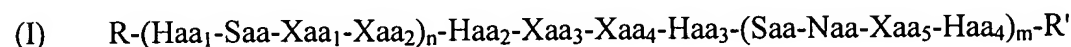
39. (Currently Amended) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 1 selected from the group consisting of:



wherein Zaa₁ and Zaa₂ are independently selected from L-aspartic acid and L-glutamic acid.

40. (Original) A conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof according to claim 39 wherein Zaa₁ and Zaa₂ are both L-glutamic acid.

41. (Currently Amended) A pharmaceutical composition comprising a conformationally constrained compound, or a pharmaceutically acceptable salt or prodrug thereof, the compound comprising an amino acid sequence (I):



[SEQ ID NO: 1-3]

wherein Haa₁, Haa₂, Haa₃ and Haa₄ are each independently an amino acid residue with a hydrophobic side chain or when n and m are both 1, one of Haa₁, Haa₂ and Haa₄ is optionally Xaa₁;

each Saa is an amino acid residue with a small side chain;

Naa is an amino acid residue with a negatively charged side chain;

Xaa₁, Xaa₂, Xaa₃, Xaa₄ and Xaa₅ are each independently an amino acid residue, Zaa₁ or Zaa₂;

R is H, an N-terminal capping group or an oligopeptide optionally capped by an N-terminal capping group;

R' is H, a C-terminal capping group or an oligopeptide optionally capped by a C-terminal capping group; and

m and n are 0 or 1, provided that at least one of m and n is 1;
wherein a conformational constraint is provided by a linker which tethers two amino acid residues, Zaa₁ and Zaa₂, in the sequence, together with one or more pharmaceutically acceptable carriers and optionally, other therapeutic and/or prophylactic ingredients.

42. (Currently Amended) An assay for identifying compounds which bind to a member of the Bcl-2 family of proteins, the assay comprising the steps of:

- (a) providing a candidate compound to be tested;
- (b) contacting a Bcl-2 family protein with the candidate compound and a peptide comprising the amino acid sequence:

IAQELRRIGDEFN [SEQ ID NO: 37]

under conditions sufficient to allow the candidate compound and the peptide to bind to the Bcl-2 family protein; and

- (c) determining whether the candidate compound has bound to the Bcl-2 family protein.

43. (Currently Amended) An assay according to claim 42 wherein the peptide has an amino acid sequence:

DLRPEIRIAQELRRIGDEFNETYTRR. [SEQ ID NO: 38]

44. (Currently Amended) A method of regulating the death of a cell, comprising contacting the cell with an effective amount of a conformationally constrained compound, or a pharmaceutically acceptable salt or prodrug thereof, the compound comprising an amino acid sequence (I):

(I) R-(Haa₁-Saa-Xaa₁-Xaa₂)_n-Haa₂-Xaa₃-Xaa₄-Haa₃-(Saa-Naa-Xaa₅-Haa₄)_m-R'

[SEQ ID NO: 1-3]

wherein Haa₁, Haa₂, Haa₃ and Haa₄ are each independently an amino acid residue with a hydrophobic side chain or when n and m are both 1, one of Haa₁, Haa₂ and Haa₄ is optionally Xaa₁;

each Saa is an amino acid residue with a small side chain;

Naa is an amino acid residue with a negatively charged side chain;

Xaa₁, Xaa₂, Xaa₃, Xaa₄ and Xaa₅ are each independently an amino acid residue, Zaa₁ or Zaa₂;

R is H, an N-terminal capping group or an oligopeptide optionally capped by an N-terminal capping group;

R' is H, a C-terminal capping group or an oligopeptide optionally capped by a C-terminal capping group; and

m and n are 0 or 1, provided that at least one of m and n is 1;

wherein a conformational constraint is provided by a linker which tethers two amino acid residues, Zaa₁ and Zaa₂, in the sequence.

45. (Currently Amended) A method of inducing apoptosis in unwanted or damaged cells comprising contacting said damaged or unwanted cells with an effective amount of a conformationally constrained compound, or a pharmaceutically acceptable salt or prodrug thereof, the compound comprising an amino acid sequence (I):

(I) R-(Haa₁-Saa-Xaa₁-Xaa₂)_n-Haa₂-Xaa₃-Xaa₄-Haa₃-(Saa-Naa-Xaa₅-Haa₄)_m-R'

[SEQ ID NO: 1-3]

wherein Haa₁, Haa₂, Haa₃ and Haa₄ are each independently an amino acid residue with a hydrophobic side chain or when n and m are both 1, one of Haa₁, Haa₂ and Haa₄ is optionally Xaa₁;

each Saa is an amino acid residue with a small side chain;

Naa is an amino acid residue with a negatively charged side chain;

Xaa₁, Xaa₂, Xaa₃, Xaa₄ and Xaa₅ are each independently an amino acid residue, Zaa₁ or Zaa₂;

R is H, an N-terminal capping group or an oligopeptide optionally capped by an N-terminal capping group;

R' is H, a C-terminal capping group or an oligopeptide optionally capped by a C-terminal capping group; and

m and n are 0 or 1, provided that at least one of m and n is 1;

wherein a conformational constraint is provided by a linker which tethers two amino acid residues, Zaa₁ and Zaa₂, in the sequence.

46. (Currently Amended) A method of treatment and/or prophylaxis of a pro-survival Bcl-2 family member-mediated disease or condition, in a mammal, comprising administering to said mammal an effective amount of a conformationally constrained compound, or a pharmaceutically acceptable salt or prodrug thereof, the compound comprising an amino acid sequence (I):

(I) R-(Haa₁-Saa-Xaa₁-Xaa₂)_n-Haa₂-Xaa₃-Xaa₄-Haa₃-(Saa-Naa-Xaa₅-Haa₄)_m-R'

[SEQ ID NO: 1-3]

wherein Haa₁, Haa₂, Haa₃ and Haa₄ are each independently an amino acid residue with a hydrophobic side chain or when n and m are both 1, one of Haa₁, Haa₂ and Haa₄ is optionally Xaa₁;

each Saa is an amino acid residue with a small side chain;

Naa is an amino acid residue with a negatively charged side chain;

Xaa₁, Xaa₂, Xaa₃, Xaa₄ and Xaa₅ are each independently an amino acid residue, Zaa₁ or Zaa₂;

R is H, an N-terminal capping group or an oligopeptide optionally capped by an N-terminal capping group;

R' is H, a C-terminal capping group or an oligopeptide optionally capped by a C-terminal capping group; and

m and n are 0 or 1, provided that at least one of m and n is 1;

wherein a conformational constraint is provided by a linker which tethers two amino acid residues, Zaa₁ and Zaa₂, in the sequence.

47. (Original) A method according to claim 46 wherein the disease or condition is an inflammatory condition, a cancer or an autoimmune disorder.

48. (Currently Amended) A method of treatment and/or prophylaxis of a disease or condition characterised by the inappropriate persistence or proliferation of unwanted or damaged cells in a mammal, comprising administering to said mammal an effective amount of a conformationally constrained compound, or a pharmaceutically acceptable salt or prodrug thereof, the compound comprising an amino acid sequence (I):

(I) $R-(\text{Haa}_1\text{-Saa-Xaa}_1\text{-Xaa}_2)_n\text{-Haa}_2\text{-Xaa}_3\text{-Xaa}_4\text{-Haa}_3\text{-(Saa-Naa-Xaa}_5\text{-Haa}_4)_m\text{-R}'$

[SEQ ID NO: 1-3]

wherein Haa₁, Haa₂, Haa₃ and Haa₄ are each independently an amino acid residue with a hydrophobic side chain or when n and m are both 1, one of Haa₁, Haa₂ and Haa₄ is optionally Xaa₁;

each Saa is an amino acid residue with a small side chain;

Naa is an amino acid residue with a negatively charged side chain;

Xaa₁, Xaa₂, Xaa₃, Xaa₄ and Xaa₅ are each independently an amino acid residue, Zaa₁ or Zaa₂;

R is H, an N-terminal capping group or an oligopeptide optionally capped by an N-terminal capping group;

R' is H, a C-terminal capping group or an oligopeptide optionally capped by a C-terminal capping group; and

m and n are 0 or 1, provided that at least one of m and n is 1;

wherein a conformational constraint is provided by a linker which tethers two amino acid residues, Zaa₁ and Zaa₂, in the sequence.